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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/740,079 | 12/18/2003 | Sharat Singh | 089.00US | 1371 |

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| EXAMINER | |
|---|---|
| SCHLAPKOHL, WALTER | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | |
| **MAIL DATE** | **DELIVERY MODE** |
| 09/10/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/740,079 | SINGH ET AL. | |
| | Examiner | Art Unit | |
| | Walter Schlapkohl | 1636 | mdf |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-23 and 28-31* is/are pending in the application.

4a) Of the above claim(s) *28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2003 and 19 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Receipt is acknowledged of the papers filed 12/30/2005, 6/30/2006, 10/25/2006, 11/7/2006 and 6/21/2007 in which claims 7, 12 & 17-18 were amended; and claims 24-27 were cancelled. Claims 1-23 and 28-31 are pending. Claims 28-31 are withdrawn. Claims 1-23 are under consideration in the instant Office action.

Any rejection of record not recited herein is hereby WITHDRAWN.

### *Drawings*

Applicant's amendment to the specification filed 6/21/2007 is acknowledged. Applicant's amendment is found remedial and the objection to the drawings is WITHDRAWN.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record.**

*Response to Arguments*

Applicant argues that structural information, for example sequence information, of an enzyme having a selected enzymatic activity would be readily available to one skilled in the art once a desired enzyme has been selected. Applicant also argues that structural information would not be required for one skilled in the art to recognize what has been invented and the claims satisfy the written description requirement in that sense. Applicant also asserts that with regard to the genus of probes/separation modifiers, Applicant need not teach what is well known in the art. Furthermore, Applicant argues that the written description requirement of the instant invention is satisfied without teaching the basic techniques of molecular biology. Applicant also argues that the disclosed species of

enzymes and probes are sufficient to enable one skilled in the art to predict the entire genus. Finally, Applicant asserts that claim 1 recites enzymes which are capable of cleaving probes into a substrate moiety and an e-tag and that given the disclosure one of ordinary skill in the art would know which enzymes these are.

Applicant's arguments have been carefully considered and are respectfully found persuasive IN PART. As set forth in the previous Office action, the claims do not provide any structural information with regard to the enzyme sequences capable of cleaving probes such that a detection group and e-tag are separated in a manner which allows the level of transcriptional response of individual cells to a potential regulatory stimulus to be determined. Neither do the claims provide any structural information regarding which probes can be used with which enzyme except for β-lactamase and the two probes set forth in Figures 6 and 8. Finally, the rejected claims encompass a set of separation modifiers as part of each e-tag reporter and no structural information is provided for a separation modifier except for those referred to in Figure 4. The art does not teach which genus of probes can be used with which genus of enzymes such that the probes can be cleaved into an e-tag and a detection group and further allowing gene expression analysis in

multiplex format on an individual cell level. Therefore, Applicant's argument that Applicant is not required to teach what is already present in the prior art is not persuasive. Applicant's argument that the disclosed species are representative of the claimed genus of probes and enzymes is not persuasive because the disclosure is limited to β-lactamase and the two probes set forth in Figures 6 and 8, and these species are not representative of the entire genus of probes and enzymes as claimed. Neither are the disclosed species sufficient to enable one skilled in the art to predict the claimed genus as Applicant asserts. Furthermore, with the exception of claims 11-14, the claims do not provide any structural characteristics with regard to the probes and enzymes used in such a method such that one of ordinary skill in the art could extrapolate from the examples those enzymes and probes that would necessarily meet the structural/functional characteristics of the rejected claims.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention. **This rejection is maintained for reasons of record.**

*Response to Arguments*

Applicant argues that the test of enablement is not whether any experimentation is required, or even whether a great deal of experimentation is required, but whether the disclosure and the art at the time of the filing date of the application are sufficient to allow one of skill in the art to practice the claimed invention without undue experimentation. Applicant further argues that one of skill in the art would be able to select an enzyme to practice the assay in spite of the large genus of enzymes due to the information provided in the instant disclosure as well as the disclosure of U.S. Patent No. 6,627,400, which was incorporated by reference at page 23, line 12 of the instant specification.

Applicant's arguments have been carefully considered and have respectfully been found unpersuasive. As explained in the previous Office action, the specification teaches two probes which can be cleaved by the enzyme β-lactamase. The specification also teaches numerous e-tag reporters which are derived from probes which can be cleaved by a nuclease. However, the specification does not teach one working example of

a method for monitoring the transcription of one or more genes in response to one or more potential regulatory stimuli comprising the recited steps of claim 1. No specific teachings are provided with regard to which transport moieties should be combined with which detection groups/separation modifiers such that the level of transcription of one or more genes can be determined by the electrophoretic mobility and level of detection group of each separated e-tag reporter. No specific teachings are provided with regard to the determination of the level of transcriptional response of each cell to the potential regulatory stimulus to which the cells were exposed and the separation of the combined e-tag reporters and how the level of transcription can be correlated. For example, how can the ACLA001 and ACLA017 e-tag reporters in Figure 4 be used to monitor the level of transcription of the gene for a kinase operatively linked to the kinase's promoter in response to one or more potential stimuli? What device would be used to separate the generated e-tag from these specific probes and how would the level of transcription be assessed, i.e. how would the "level of detection group of each separated e-tag reporter from the ACLA001 and ACLA017 probes and their respective electrophoretic mobility" determine the transcription level of the kinase operatively linked to the kinase's promoter? Could

any enzyme or even any nuclease be used in any cell in which the experiment were performed? These deficiencies are not overcome by the disclosure of U.S. Patent 6,627,400, incorporated by reference into Applicant's instant specification. Therefore, Applicant's argument that one of ordinary skill in the art would be able to select an enzyme to practice the assay in spite of the large genus of enzymes due to the information provided in the instant disclosure as well as the disclosure of U.S. Patent No. 6,627,400 is not found persuasive. Furthermore, Examiner has never contended that the instant claims were not enabled solely because experimentation (even a great deal of experimentation) is required. Given the analysis of the Wands factors set forth in the prior Office action including the state of the prior art, the nature of the invention, the guidance provided by the specification, and the unpredictability of the art, it is clear that one skilled in the art would be required to conduct an undue and burdensome amount of experimentation to determine which enzymes could be used with which probes in order to monitor the level of transcription of one or more genes in response to one or more potential regulatory stimuli. This unpredictability is exacerbated by the large genus of enzymes and probes claimed.

*Conclusion*

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative.

NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Joseph Woitach can be reached at (571) 272-0739.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

August 31, 2007

DAVID GUZO
PRIMARY EXAMINER